BRIEF COMMUNICATION

Characteristics of Ascites in Patients With Pregnancy-Specific Liver Diseases

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BACKGROUND & AIMS: The characteristics of ascites in patients with pregnancy-specific liver disease (PsLD), which comprise acute fatty liver of pregnancy, hemolysis, increased levels of liver enzymes, low platelet syndrome, and preeclampsia-associated liver dysfunction, are unknown. We evaluated the cellular and biochemical characteristics, and model for end-stage liver disease scores, in patients with PsLD. **METHODS:** We evaluated 46 consecutive patients with PsLD for the presence of ascites. We assessed cellular and biochemical characteristics of the ascites fluid from these patients. **RESULTS:** Ascites was observed in 35 of 46 patients with PsLD (76%). In 25 patients tested (71.4%), the ascites fluid had low levels of albumin (<0.2 g/dL) and protein (<1 g/dL) and high serum ascites albumin gradients, indicating portal hypertension. Spontaneous bacterial peritonitis was observed in 48% of patients tested and was not associated with mortality. Patients with ascites had significantly low serum levels of protein and albumin ($P < .001$). Model for end-stage liver disease scores did not differ between patients with or without ascites (32 vs 27; $P = .1$). **CONCLUSIONS: Ascites occur in 76% of women with PsLD, is transient, and has characteristics of portal hypertension, based on high serum ascites albumin gradients. Almost half of patients with PsLD develop spontaneous bacterial peritonitis, which does not affect survival.**

Keywords: AFLP; HELLP; Hepatitis; Diagnostic Factors; Paracentesis.

Ascites and spontaneous bacterial peritonitis (SBP) are complications seen commonly among patients with cirrhosis,[1] but rarely in patients with acute viral hepatitis unless complicated by acute liver failure.[2] Ascites can rarely complicate the course of patients with pregnancy-specific liver diseases (PsLD) such as preeclampsia, hemolysis, elevated liver enzyme, and low platelets (HELLP) syndrome, and acute fatty liver of pregnancy (AFLP).[3–6] In addition, ascites is an important diagnostic criterion in AFLP,[7] and in distinguishing PsLD from viral hepatitis.[8] Ascites is a negative predictor of survival.[8]

The recognition of ascites in PsLD can be dated back to 1949, when Golden[9] first drew attention to its rarity. He described ascites in a patient with liver insufficiency and preeclampsia from a series of 55,000 pregnancies. Since then, studies have reported ascites in 5% to 10% of patients with HELLP syndrome.[3,4,6,10] Its presence connotes severe disease with significant morbidity, including respiratory distress, postpartum complications, and death.[8,10]

To date, little attention has been paid to the characteristics of ascites in patients with PsLD. Although the presence of ascites has intrigued physicians since the description by Golden[9] in 1949, the only attempt at characterizing ascites was performed by Calvin et al[11] in 1991 in a series of 9 patients who underwent cesarean section. Information regarding its cellular and biochemical features are scanty. Moreover, its presence often leads to diagnostic confusion such that internists, gastroenterologists, and hepatologists often are called upon to provide medical advice, particularly with regard to its etiology and treatment. In addition, the frequency, impact, and outcome of associated SBP in such patients are unknown.

Therefore, we undertook this study to evaluate the characteristics of ascites in patients with PsLD and to assess the impact of SBP on the outcome. We also aimed to determine the association of the model for end-stage liver disease (MELD) score with ascites.

Patients and Methods

The present study focused on only a subset of patients with ascites among all patients with PsLD, which was reported recently.[8] The current study analyzed the clinical, biochemical, and microbiologic characteristics of patients with ascites among the 46 consecutive patients with PsLD during the period from January 2000 to July 2003. The detailed methods of the study were described recently.[8] Very briefly, because of substantial overlap in the clinical features and laboratory abnormalities in patients with the clinical diagnosis of preeclampsia, HELLP syndrome, and AFLP, patients were grouped together as previously reported.[8] All patients underwent routine hematologic and serum biochemical tests as well as abdominal ultrasonography for assessment of the liver, portal vein, spleen, and presence of ascites. Ascitic fluid paracentesis was performed and fluid was analyzed for cell count, type, albumin, and protein in all patients who underwent paracentesis. Ascitic fluid culture was performed by inoculation of blood culture bottles with 10 mL of ascitic fluid. SBP was defined as a total neutrophil count of 250 cells/mm^3 with or without a positive culture. Patients were followed for up to 5 years after discharge or death during admission. The MELD score was calculated as reported.[12]

Abbreviations used in this paper: AFLP, acute fatty liver of pregnancy; HELLP, hemolysis, elevated liver enzyme, and low platelets; MELD, model for end-stage liver disease; PsLD, pregnancy-specific liver disease; SAAG, serum-ascites albumin gradient; SBP, spontaneous bacterial peritonitis.

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Table 1. Comparison of Clinical and Laboratory Features Between Patients With and Without Ascites

Variable	Ascites (n = 35), median (range)	No ascites (n = 11), median (range)	*P* value
Age, *y*	23 (18–40)	25 (21–29)	.068
Gestation age, *wk*	34 (8–40)	36 (30–38)	.027
Systolic BP, *mm Hg*	150 (90–200)	160 (120–200)	.491
Diastolic BP, *mm Hg*	100 (60–160)	100 (70–140)	.825
Serum creatinine, *mg/dL*	2.5 (1–6.7)	1.6 (1–7.8)	.027
Blood glucose, *mg/dL*	72 (7–191)	63 (46–115)	.94
Serum total protein, *g/dL*	5.2 (3.2–6.5)	5.9 (5.3–6.6)	<.001
Serum albumin, *g/dL*	2.25 (1.3–3)	2.7 (2.6–2.9)	<.001
Bilirubin, *mg/dL*	10.6 (1–31.6)	6.0 (2.2–15.1)	.255
AST, *U/L*	148 (40–1396)	188 (58–893)	.920
ALT, *U/L*	168 (26–529)	208 (63–446)	.698
ALP, *U/L*	309 (91–1099)	657 (198–1653)	.021
Prothrombin time, *s*	26 (14–98)	24.5 (13–60)	.233
Hemoglobin, *g/dL*	9.9 (0.5–15.5)	11.1 (5.1–17)	.091
WBC, 10^3/*dL*	18.7 (1.5–203)	14 (4.22–147)	.271
Platelets, 10^3/*dL*	37.0 (5–153)	45 (10–75)	.702
Blood urea, *mg/dL*	47.5 (10–120)	31 (17–156)	.111
Serum sodium, *mEq/L*	135 (113–148)	137 (114–143)	.254
Uric acid, *mg/dL*	8.3 (4.2–13.6)	6.8 (5.1–17.4)	.419
MELD score	30.38 (10.0–41.8)	25.2 (11.14–36.6)	.104
INR	2.25 (1.17–8.17)	1.9 (1.08–5)	.229

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BP, blood pressure; INR, international normalized ratio; WBC, white blood cell count.

Statistical Analysis

Data were summarized using medians and ranges for continuous or numeric variables and percentages and counts for categoric variables. A comparison of continuous variables was performed using the Student *t* test or the Mann–Whitney *U* test, and the chi-square test was used to compare categoric variables. A *P* value less than .05 was considered significant. Statistical analysis of data was performed with SPSS (version 16; SPSS, Inc, Chicago, IL).

Results

Of the 46 patients with PsLD, 35 had clinical and ultrasound evidence of ascites. The clinical features and demographics of patients with and without ascites is summarized in Table 1. Four patients with ascites underwent ascitic paracentesis before delivery, 2 for diagnostic purposes and the other 2 for therapeutic purposes (2 L of paracentesis for respiratory distress and painful abdominal distention, respectively). Ten patients underwent aspiration of ascitic fluid during an emergency Cesarean section (0.5–3 L) and 7 patients underwent paracentesis post partum (3 diagnostic and 4 therapeutic of 3–5 L). Four patients underwent 2 or more paracentesis procedures, all post partum. There was no difference in the clinical and laboratory features in the ascites and nonascites group except for low serum albumin and serum protein levels in the ascites group (Table 1). Similarly, there was no difference between the SBP and non-SBP group except for hyponatremia, which was significantly more common in the SBP group (Table 2). In patients with a high leukocyte count in ascitic fluid, there was no clinical or radiologic evidence of secondary peritonitis. Two patients had blood-tinged paracentesis and the corrected polymorphonuclear counts in these 2 patients were less than 250, and hence were not included as SBP.[13] *Escherichia coli* was isolated in ascitic fluid culture in 4 of 12 patients with SBP. Overall, blood culture was sent in 20 patents with ascites and was positive for *E coli* (n = 4) and *Klebsiella pneumoniae* (n = 2) in 6 patients with ascites, including 3 of the earlier-described 4 patients with SBP.

The MELD score in those with and without ascites and in those with and without SBP are shown in Tables 1 and 2 and did not differ significantly.

Follow-up evaluation for up to 5 years did not show any evidence of liver dysfunction either clinically or ultrasonologi-

Table 2. Comparison of Ascitic Fluid and Laboratory Features Between Patients With and Without SBP

Variable	SBP (n = 12), median (range)	No SBP (n = 13), median (range)	*P* value
Ascitic fluid WBC count, *cells/mm*^{3}	2250 (800–20,800)	200 (9–1200)	NA
Ascitic fluid neutrophil count, *cells/mm*^{3}	2190	25	
Ascitic fluid lymphocyte count, *cells/mm*^{3}	320	66	
Ascitic fluid protein, *g/dL*	0.9 (0.2–2)	0.6 (0.1–1)	.049
Ascitic fluid albumin, *g/dL*	0.2 (0–0.6)	0.1 (0–0.2)	.017
Serum sodium, *mEq/L*	128 (113–142)	135 (126–148)	.015
MELD score	32.9 (26–48.5)	32.7 (10–40)	.049

NA, not applicable; WBC, white blood cell.

cally. Five patients who conceived again underwent successful pregnancies and had uneventful full-term deliveries without recurrence of ascites.

Discussion

Pregnancy-specific liver diseases such as AFLP, HELLP syndrome, and preeclampsia with liver dysfunction are an important cause of acute liver disease in pregnancy. Complications of these conditions can result in substantial morbidity and mortality, including acute liver failure. There is a paucity of studies on the characteristics of ascitic fluid among patients with PsLD, and our study is one of the few efforts to investigate this in such patients. Although ascites is reported in up to 10% of patients in some Western series,[3,4,10] in our earlier publication we noted ascites in 76% of our patients with PsLD.[8] The difference we found in our study could be owing to the advanced and severe disease at the time of presentation as reflected in the high MELD score. The current report highlights the characteristics of ascites in these patients. We also noted SBP in 12 of 25 (48%) patients in whom it was investigated.

In our series, the ascitic fluid was characterized by low protein and albumin levels and is similar to that reported by Calvin et al[11] in their series of 9 patients with preeclampsia and HELLP syndrome. In our series, all patients had a high serum-ascites albumin gradient (SAAG), suggesting portal hypertension as a cause of ascites. Calvin et al[11] classified their patients as having "transudate" ascites, and speculated ascites were caused by portal hypertension. Although SBP was noted in half of our patients with ascites, SBP did not impact survival, which is consistent with a report of SBP in patients with fulminant hepatic failure.[2]

The high SAAG noted in patients with ascites and PsLD suggests the presence of portal hypertension, albeit transient in the pathogenesis of this disorder. Transient portal hypertension may be owing to the convergence of various related factors that include vasospasm and profound vascular endothelial cell dysfunction particularly of liver and kidneys,[11,14] and plugging of the liver sinusoids by red blood cells, platelets, and fibrin. In addition, hepatocyte microvesicular swelling and liver cell collapse may aggravate portal hypertension further.[15–18] Furthermore, the hemodynamic alterations in such patients are similar to those noted in patients with portal hypertension, including increased sinusoidal pressure. In the only 4 patients with pregnancy-specific liver disease with ascites in whom a hepatic vein pressure study was ever performed, the hepatic venous pressure gradient was increased in all 4 patients, thereby confirming a sinusoidal cause for portal hypertension.[19] Maternal microvascular endothelial dysfunction may be central to the pathogenesis of many of the manifestations, including portal hypertension in patients with PsLD.[20] As noted in some of our patients, ascites may be appreciated only after delivery in patients with the HELLP syndrome. Similar reports exist,[19,21] including a particular dramatic case report by Foreman,[21] in which up to 12 L were drained after delivery. These changes are transient, lasting days, and resolve once the primary condition is corrected, as shown in serial liver biopsies in a patient with AFLP.[18] Sinusoidal obstruction produced by fatty deposition resolves after delivery, thus illustrating the transient nature of the disease.[18] The absence of ascites during a follow-up period of up to 5 years in our series and also during succeeding pregnancies in 5 women appear to suggest that these conditions are confined to PsLD and not caused by chronic liver disease. Furthermore, post mortem liver biopsy features in 10 of our patients did not show any evidence of chronicity; instead, features of fatty changes, spotty necrosis, and hemorrhage were noted.

The shortcomings of our study included the inherent limitation present in any retrospective study. Other shortcomings included the absence of measurement of cardiac indexes, which may be abnormal in some of these patients.[6] Furthermore, because ascitic fluid analysis could not be performed in all patients, the incidence of SBP may be over-represented in this series. However, these limitations are offset by the detailed characteristics of ascitic fluid in a relatively large number of patients with PsLD, an area in which there are almost no data.

In conclusion, our attempt at studying the cellular, biochemical, and microbiologic characteristics of ascites in patients with PsLD adds insight into the mechanism of ascites in PsLD. The presence of a high SAAG in patients with PsLD underscores the contribution of sinusoidal portal hypertension as a cause of ascites. Although spontaneous bacterial peritonitis developed in almost half of the patients with PsLD, this did not affect survival. The MELD score was similar in patients with or without SBP.

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Reprint requests

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Conflicts of interest

The authors disclose no conflicts.